March 5, 2007

Lynne Jones
Metal Carboxylates Coalition
SOCMA
1850 M Street NW, Suite 700
Washington, DC 20036

Dear Ms. Jones,

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for the revised Calcium dipropionate submission, posted on the ChemRTK HPV Challenge Program Web site on September 22, 2004. I commend the Metal Carboxylates Coalition for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Coalition advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact me at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

*/s/*

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: O. Hernandez
C. Augustyniak
J. Willis

**EPA Comments on Chemical RTK HPV Challenge Submission:**
**Calcium dipropionate**

## Summary Of EPA Comments

The sponsor, the Metal Carboxylates Coalition, submitted a revised test plan and robust summaries to EPA for Calcium dipropionate (CAS No. 4075-81-4), dated September 10, 2004. EPA posted the submission on the ChemRTK HPV Challenge Web site on September 22, 2004. Data were also submitted for a proposed analog, propionic acid (CAS No. 79-09-4).

EPA has reviewed this submission and has reached the following conclusions:

1. Analog Justification. The submitter's use of propionic acid as an analog for calcium dipropionate is reasonable.

2. Physicochemical Properties. Adequate data were submitted for these endpoints for the purposes of the HPV Challenge Program.

3. Environmental Fate. The submitter needs to provide Model III fugacity results for propionic acid.

4. Health Effects. The submitted data for acute, repeated-dose and genetic toxicity endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgment on the adequacy of the reproductive and developmental toxicity endpoints pending submission of information on the reproductive organs evaluation from an adequate repeated-dose toxicity study and a justification for dose selection for the developmental toxicity studies.

5. Ecological Effects. Adequate data were submitted for these endpoints for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

## EPA Comments On The Calcium Dipropionate Challenge Submission

### Analog Justification

Although the submitter did not provide an adequate technical discussion on dissociation of calcium dipropionate (for example, did not distinguish between the pKa and the dissociation constant for the metal-ligand complex), EPA agrees that for the purposes of the HPV Challenge Program, propionic acid is an appropriate analog for calcium dipropionate, given the published stability constant (log $K_1$) for calcium propionate of 0.5 (located by EPA: Furia, 1972), similar water solubility values for calcium dipropionate and propionic acid, and an expectation that significant dissociation of the salt will occur at neutral pH.

### Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, water solubility and partition coefficient)

Adequate data were provided for these endpoints for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation and fugacity)

The data provided for the photodegradation and biodegradation endpoints are adequate for the purposes of the HPV Challenge Program.

*Stability in water.* The dissociation data provided by the submitter are adequate for the purposes of the HPV Challenge Program, if augmented with a robust summary for the stability constant data in Furia (1972).

*Fugacity.* The submitter needs to provide level III fugacity modeling data for propionic acid. A Henry's Law constant alone is not sufficient.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for acute, repeated-dose and genetic toxicity endpoints are adequate for the purposes of the HPV Challenge Program. EPA reserves judgment on the adequacy of the reproductive and developmental toxicity endpoints pending submission of information on the reproductive organs evaluation from an adequate repeated-dose toxicity study and a justification for dose selection for the developmental toxicity studies.

*Reproductive/Developmental toxicity.* No reproduction toxicity studies have been conducted with Ca dipropionate. EPA agrees that the results of repeated-dose toxicity studies and available developmental toxicity studies should address these endpoints. However, (1) none of the robust summaries for repeated-dose toxicity studies provides a list of reproductive organs that were weighed and/or evaluated histopathologically and (2) the dose levels used in the developmental toxicity studies were significantly lower (300-400 mg/kg/day) than recommended (1000 mg/kg/day) for this type of study by the OECD guidelines. Because neither maternal nor developmental toxicity was evident at these doses, a justification for dose selection is needed.

Ecological Effects (fish, invertebrates, and algae)

EPA agrees that data from the analog, propionic acid, adequately represent the aquatic hazard of calcium dipropionate.

## Specific Comments on the Robust Summaries

General

In general, the robust summaries provided by the submitter included too few study details. EPA refers the submitter to guidance on developing robust summaries for the HPV Challenge Program that can be found at the following website: http://www.epa.gov/chemrtk/pubs/general/robsumgd.htm.

Environmental Fate

*Stability in water*. The submitter needs to rename Section 3.1.2 in the IUCLID Data Set for calcium propionate as "Stability in Water – Dissociation".

Health Effects

In the IUCLID Data Set for Propionic acid, Calcium salt, the submitter needs to prepare and incorporate an individual robust summary for each study discussed in the additional references sections. Section 5.11 of the IUCLID Data Set for propionic acid, which is not essential for this submission, needs to be translated into English or deleted.

*Genetic toxicity (gene mutations).* Missing robust summary information includes: identity of the positive controls used, criteria used to evaluate a positive or negative response, detailed description of the method.

*Reproductive toxicity*. Histopathological data relating to the reproductive organs from the repeated-dose studies need to be included in this section.

## Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

## References

Furia, T.E 1972. Sequestrants in foods. In *CRC* Handbook of Food Additives, 2nd ed. Online at http://www.coldcure.com/html/stability_constants.html.